Notice of Allowability	Application No.	Applicant(s)	
	10/693,538	SANICOLA-NADEL ET AL.	
	Examiner	Art Unit	
	Parithosh K. Tungaturthi	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *05/01/2007*.

2. ☒ The allowed claim(s) is/are *46, 44, 47, 48, 50, 59, 60, 62-77 and 81-285 (Renumberred 1-228, respectively)*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER

EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

2. Authorization for this examiner's amendment was given in a telephone interview with Ms. Megan E. Williams on 07/18/2007.

Amendments to the claims

3. The amendments to claims 46, 47, 62, 70-77, 81, 82 and 86 are as follows:

Claim 46 - A method of treating a subject having a tumor that over-expresses Cripto comprising administering to the subject a composition comprising a monoclonal antibody that specifically binds to an epitope of Cripto comprised in the domain spanning amino acid residues from about amino acid 46 to about amino acid 62 of SEQ ID NO:1 or about amino acid residues from about amino acid 46 to about amino acid 62 of SEQ ID NO:2 in an effective amount.

Claim 47 - A method of treating a subject having a tumor that over-expresses Cripto comprising administering to the subject a composition comprising a monoclonal

antibody that specifically binds to an epitope of Cripto comprised in the cysteine-rich domain of Cripto spanning from about amino acid residue 114 to about amino acid residue 150 of SEQ ID NO:1 or from about amino acid residue 114 to about amino acid residue 150 of SEQ ID NO:2 in an effective amount.

Claim 62 - A method of inhibiting proliferation of tumor cells that express Cripto in a subject comprising the step of administering to the subject an effective amount of a composition comprising a monoclonal antibody that specifically binds to an epitope of Cripto comprised in the domain spanning amino acid residues from about amino acid 46 to about amino acid 62 of SEQ ID NO:1 or from about amino acid 46 to about amino acid 62 of SEQ ID NO:2 and a pharmaceutically acceptable carrier.

Claim 70 - A method of inhibiting proliferation of tumor cells that express Cripto in a subject comprising the step of administering to the subject an effective amount of a composition comprising a monoclonal that specifically binds to an epitope of Cripto comprised in the domain spanning amino acid residues from about amino acid 46-62 of SEQ ID NO:1 or amino acid residues from about amino acid 46-62 of SEQ ID NO:2, wherein the antibody is conjugated to a maytansinoid, and a pharmaceutically acceptable carrier.

Claim 71 - A method of inhibiting proliferation of tumor cells that express Cripto in a subject comprising the step of administering to the subject an effective amount of a

composition comprising a monoclonal antibody that binds to Cripto, wherein the antibody is a humanized version of the antibody produced by the hybridoma B3F6.17.

Claim 72 - A method of inhibiting proliferation of tumor cells that express Cripto in a subject comprising the step of administering to the subject an effective amount of a composition comprising a monoclonal antibody that specifically binds to an epitope of Cripto to which an antibody produced by hybridoma B3F6.17 binds, and a pharmaceutically acceptable carrier.

Claim 73 - A method of inhibiting proliferation of tumor cells that express Cripto in a subject comprising the step of administering to the subject an effective amount of a composition comprising a monoclonal antibody, wherein the antibody specifically binds to an epitope of Cripto selected from the group of epitopes to which antibodies produced by hybridomas of A27F6.1 and B3F6.17 bind, and is capable of internalizing Cripto.

Claim 74 - A method of inhibiting proliferation of tumor cells that express Cripto in a subject comprising the step of administering to the subject an effective amount of a composition comprising a monoclonal antibody that specifically binds to an epitope of Cripto comprised in the cysteine-rich domain of Cripto spanning from about amino acid residue 114 to about amino acid residue 150 of SEQ ID NO:1 or from about amino acid

residue 114 to about amino acid residue 150 of SEQ ID NO:2, and a pharmaceutically acceptable carrier.

Claim 75 - A method of inhibiting proliferation of tumor cells that express Cripto in a subject comprising the step of administering to the subject an effective amount of a composition comprising a monoclonal antibody that binds to Cripto, wherein the antibody specifically binds to an epitope of Cripto selected from the group of epitopes to which antibodies produced by hybridomas of A6.C12.11, A8G3.5, and A6F8.6 bind, and a pharmaceutically acceptable carrier.

Claim 76 - A method of inhibiting proliferation of tumor cells that express Cripto in a subject comprising the step of administering to the subject an effective amount of a composition comprising a monoclonal antibody that specifically binds to a Cripto amino acid sequence shown in SEQ ID NO: 1 or SEQ ID NO:2 and inhibits the interaction of Cripto and ALK4.

Claim 77 - A method of inhibiting proliferation of tumor cells that express Cripto in a subject comprising the step of administering to the subject an effective amount of a composition comprising a monoclonal antibody that binds specifically to an epitope of Cripto selected from the group of epitopes to which antibodies produced by hybridomas A6C12.11, A6F8.6, A8G3.5, A19A10.30, A10B2.18, A17A2.16, and B3F6.17 bind, and a pharmaceutically acceptable carrier.

Claim 81 - A method of inhibiting proliferation of tumor cells that express Cripto in a subject comprising the step of administering to the subject an effective amount of a composition comprising a monoclonal antibody that binds to Cripto, wherein the antibody specifically binds to an epitope of Cripto to which an antibody produced by hybridoma A10B2.18 binds, and a pharmaceutically acceptable carrier.

Claim 82 - A method of treating a subject having a tumor that over-expresses Cripto comprising administering to the subject a composition comprising a monoclonal antibody that specifically binds to an epitope of Cripto comprised in the domain spanning amino acid residues from about amino acid 46-62 of SEQ ID NO: 1 or amino acid residues from about amino acid 46-62 of SEQ ID NO:2, wherein the antibody is conjugated to a maytansinoid, in an effective amount.

Claim 86 - A method of treating a subject having a tumor that over-expresses Cripto comprising a monoclonal antibody, wherein the antibody specifically binds to an epitope of Cripto selected from the group of epitopes to which antibodies produced by hybridomas of A27F6.1 and B3F6.17 bind, and is capable of internalizing Cripto.

Reasons for allowance:

4. The specification provides sufficient information for the epitopes that the claimed antibodies bind to, in addition to that such antibodies modulate Cripto signaling and modulate tumor growth. The invention also provides guidance that the antibodies which

bind to the domains spanning amino acid residues 46-62 of SEQ ID NO:1, 46-62 of SEQ ID NO:2, 114-150 of SEQ ID NO:1 and 114-150 of SEQ ID NO:2 modulate Cripto signaling and tumor growth (paragraphs 9-21, in particular); in addition to that such antibodies also block the interaction between Cripto and ALK4 (paragraph 8, in particular). The specification, in paragraph 42, states that the antibodies produced by the hybridomas A27F6.1 and B3F6.17 are capable of internalizing Cripto.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Parithosh K. Tungaturthi whose telephone number is 571-272-8789. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Respectfully,
Parithosh K. Tungaturthi, Ph.D.
Ph: (571) 272-8789

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER